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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/117,810	05/12/99	SCHUTZ G	012627-007

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BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA VA 22313-1404

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EXAMINER	
LU,F	

ART UNIT	PAPER NUMBER
1655	11

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/117,810	Schutz et al.,
Examiner	**Art Unit**
Frank Lu	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 12, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *5-9* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *5-9* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 6-9 are dependent on claim 5.

Claim 5 are rejected as vague and indefinite because it is unclear what it intended. For example, how to use primers, antibodies and DNA in (a)-(c) in investigation and monitor of spermatogenesis?

3. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to use primers, antibodies and DNA in (a)-(c) in investigation and monitor of spermatogenesis.

Claim Rejections - 35 U.S.C. § 102/103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 5 and 7 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Delmas *et al.*, (Mol. Endocrinol. 7, 1502-1514, November 1993).

Delmas *et al.*, teach induction of cAMP-responsive element modulator (CREM) activator proteins in spermatids and their down-stream targets. They showed that CREM tau was efficiently phosphorylated at a serine residue at position 117 by the protein kinase-A endogenous to germ cells. This indicated that CREM tau constitutes a natural target of the adenylyl cyclase pathway during spermatogenesis. The phosphorylated CREM tau became a powerful activator. The rise in CREM tau protein coincided with the transcriptional activation of several genes such as the male germ cell-specific RT7. The RT7 promoter was shown to be cAMP inducible and

activated by CREM tau in transfection assays (page 1502, abstract). Using Western and Northern analysis, they further showed that R7 RNA appeared on exactly the same day as CREM proteins were first produced. As a control, the same Northern blot was hybridized with an actin probe to show that comparable amounts of RNA were loaded in each lane (as a standard reagent). These experiments revealed a good correlation between CREM protein synthesis and RT7 transcription activation (first paragraph of left column in page 1509 and Figure 6). In cotransfection experiments, CREMτ expression vector and a reporter chloramphenicol acetyl transferase (CAT) vector containing the RT7 promoter cAMP-responsive element (CRE) were cotransfected into human choriocarcinoma JEG-3 cells. Coexpression of CREMτ enhanced activation of the RT7 CRE by cAMP. Thus the RT7 CRE is functional and potentially represents a cellular target of CREM transregulatory function (second paragraph of left column in page 1509 and Figure 7 in page 1510). Note that CREM-specific antibodies blocked RT7 *in vitro* transcription (page 1502, abstract). The examiner considered that the reference of Delmas *et al.*, taught the step of puncturing the animal's testis since isolated germ cells were prepared from adult Sprague-Drawley rat (see page 1512, left column). Although Delmas *et al.*, did not directly show monitoring spermatogenesis using CREM and /or CREM-dependent protein as described in claim 5, in the absence of convincing evidence to the contrary the claimed invention, this limitations is considered as inherent to the reference taught by Delmas *et al.*, since it has been well known that CREM has a pivotal role during the developmental process of male germ cells (ie.,spermatogenesis) (see a review by Delmas *et al.*, Mol. Cell. Endocrinology, 100, 121-124, 1994).

Response to Arguments

In page 5, third paragraph of applicant's remarks, applicant argued that " Delmas et al could not possibly disclose or suggest detecting and monitoring the presence of CREM and/or CREM-dependent proteins as a means of investigating and monitoring spermatogenesis in a male animal" since (1) "Delmas et al do not disclose or suggest that if CREM is not expressed, or is expressed to a reduced extent but not in a phosphorylated form, the CREM-dependent proteins are not expressed, or are expressed to a reduced extent"; and (2) "Delmas et al do not disclose or suggest that such conditions would result in unbalanced spermatogenesis and ultimately non-functioning spermia".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, in response to applicant's arguments that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., CREM is not expressed, or is expressed to a reduced extent but not in a phosphorylated form, the CREM-dependent proteins are not expressed, or are expressed to a reduced extent) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Second, since the reference showed the detection of the expression of CREM and/or CREM-dependent protein (i.e., R7) and it has been well known that spermatogenesis includes before and after meiosis of germ cells (see a review by Delmas *et al.*, Mol. Cell. Endocrinology, 100, 121-124, 1994), the examiner considered that Delmas *et al.*, did taught the process of investigating spermatogenesis. Third, although

Delmas *et al.*, did not directly show monitoring spermatogenesis using CREM and /or CREM-dependent protein as described in claim 5, in the absence of convincing evidence to the contrary the claimed invention, this limitations is considered as inherent to the reference taught by Delmas *et al.*, since it has been well known that CREM has the pivotal role during the developmental process of male germ cells (see a review by Delmas *et al.*, Mol. Cell. Endocrinology, 100, 121-124, 1994).

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Delmas *et al.*, (1993) as applied to claims 5 and 7 above, and further in view of Bocker *et al.*, (Cell Tissue Res. 278, 595-600, 1994).

The teaching of Delmas *et al.*, have been summarized previously, *supra.*

Delmas *et al.*, do not disclose to investigate and monitor spermatogenesis in a male human.

Bockers *et al.*, teach the localization of FSH immunoreactivity and hormone receptor mRNA in testicular tissue of infertile man using testicular biopsy (see abstract in page 595, right column in page 595, and left column in page 596).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have investigated and monitored spermatogenesis using the method of Delmas *et al.*, in a male human as suggested by Bockers *et al.*. One having ordinary skill in the art would have motivated to use method of Delmas *et al.*, in a male human because the application of a known method in a male human instead of a male rat would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

9. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delmas *et al.*, (1993) as applied to claims 5 and 7 above, and further in view of Stratagene Catalog (1988, page 39).

The teachings Delmas *et al.*, of have been summarized previously, *supra.* Note that expression vectors could be considered as carriers and conventional vehicles (see page 1512, left column).

Delmas *et al.* do not disclose a kit.

The Stratagene catalog (page 39) discloses the general concept of kits for performing gene characterization assays and discloses the advantages of kits. The kit format is utilized not only assemble a variety of different reagents together but ensure the quality and compatibility of the reagents.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized the components and method taught by Delmas *et al et al.*, into a kit because the method for investigating and monitoring a process of spermatogenesis was conventional at that time the inventions were made and the kit format was utilized not only assemble a variety of different reagents together but ensured the quality and compatibility of the reagents. The Stratagene Catalog 1988 would have motivated and suggested the assemblage of reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages, thus resulting in instant kit described in claims 8 and 9. One having ordinary skill in the art at the time the

invention was made would have been a reasonable expectation of success to combine these prior art together because all of these prior art are known and are easy to use.

Response to Arguments

10. Applicant's arguments with respect to claims 3 and 4 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. No claim is allowed.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank L., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
April 19, 2001

Ethan Whisenant, Ph.D.
Primary Examiner (FSA